

Application Number: 10/810,296. Art Unit: 1631. Reply to Office Action of 02/27/07

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1 (Original): A multiparameter method of screening for the diagnosis, the prevention or the treatment of atherosclerosis-related coronary heart disease (CHD) or stroke comprising;

defining the disease as atherosclerosis-related CHD or stroke;

defining the normal as free from said disease;

defining the following parameters as

atherosclerotic parameters consisting of c = the Low-density lipoprotein (LDL) concentration parameter in mg/dL or c = the C-reactive protein (CRP) concentration parameter in mg/L, p = the blood systolic pressure parameter in mmHg or p = the blood diastolic pressure parameter in mmHg, f = the heart rate parameter in s^{-1} , a = the radius parameter along arterial radius in cm, T = the temperature parameter of

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blood plasma in °C, α = the angle parameter between gravity and the mean velocity of blood fluid in arterial vessels in degree and z = the axial position parameter of diffusional flux along the inner wall in the axial direction of arterial vessels in cm, called diffusional length;

an individual having the measured values of said atherosclerotic parameters of the following expressions:

$$J = A c^{\frac{11}{9}} (v^3 D^{16})^{\frac{1}{27}} \left(\frac{g \cos \alpha + fu}{z} \right)^{\frac{2}{9}} \quad (1.1)$$

or

$$J = B c^{\frac{11}{9}} p^{\frac{1}{3}} T^{\frac{16}{27}} a^{\frac{2}{3}} f^{\frac{2}{9}} z^{-\frac{2}{9}} \quad (1.2)$$

and

$$J = E c^{\frac{11}{9}} D^{\frac{16}{27}} z^{-\frac{2}{9}} (\cos \alpha)^{\frac{2}{9}} \quad (1.3)$$

wherein J = the mass transfer flux in 10^{-5} g/(cm²s), A , B and E = the constants of conversion factors, v = the eddy velocity of blood fluid in arterial vessels in cm/s, u = the mean velocity of the blood fluid in cm/s, D = the diffusion coefficient in cm²/s, and g = the gravitational acceleration in cm/s²;

the individual having the normal values of said

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atherosclerotic parameters;

determining the disease risks yielded by the differences between said measured values and said normal values of said atherosclerotic parameters;

adding all said disease risks together yields a total risk of said disease;

determining a disease risk level containing said total risk of said disease;

selecting an atherosclerotic risk factor related to an atherosclerotic parameter that is the greatest contribution to said total risk of said disease so as to result in said risk factor as a primary therapy target of said disease;

selecting a greater flux between the LDL mass transfer flux and the monocyte mass transfer flux so as to result in said greater flux as a primary cause in said disease;

selecting a greater concentration level between the LDL level in serum and the CRP level in

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blood plasma so as to result in said greater level as a secondary therapy target of said disease;

determining a relative ratio between currently said total risk and previously said total risk so as to yield said relative ratio as a therapeutic efficacy of said disease;

repeating above-mentioned said methods until said disease risk level is reduced to a normal level for said individual who requires the therapy to prevent or to treat atherosclerosis-related CHD or stroke; and

above-mentioned said methods are written as an executable computer program named the MMA.exe, or another name, to be installed into a general purpose digital computer device to accomplish said methods and to output a result of said methods to a display or a memory or another computer on a network, or to a user.

Claim 2 (Original): A method as in claim 1 wherein determining said disease risk yielded by the difference between the measured value and the normal value of said LDL concentration parameter, said

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method comprising the steps of:

a measured value, c_m in mg/dL, of the individual's LDL concentration in human serum is determined using a medical technique for measuring the concentration of blood constituents or said c_m is determined by the physician;

a normal value, c_n in mg/dL, of said LDL concentration is determined by the physician or said $c_n = 100$ mg/dL for adult;

substituting said c_m and said c_n into the following expression where $c_m \geq c_n$:

$$R_1 = \left(\frac{c_m}{c_n} \right)^{\frac{11}{9}} - 1 \quad (1)$$

and

calculating (1) yields said disease risk R_1 caused by said LDL concentration parameter related to the atherosclerotic risk factors being an elevated LDL concentration in human serum, high-fat diet, hypercholesterolemia or other risk factors that increase said LDL concentration.

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Claim 3 (Original): A method as in claim 1 wherein determining said disease risk yielded by the difference between the measured value and the normal value of said CRP concentration parameters, said method comprising the steps of:

a measured value, c_m in mg/L, of the individual's CRP concentration in human blood plasma is determined using a medical technique for measuring the concentration of blood constituents or said c_m is determined by the physician;

a normal value, c_n in mg/L, of said CRP concentration and an equivalent factor, F , are determined by the physician wherein $F = \left(\frac{D_c}{D_L} \right)^{\frac{16}{27}}$,

D_c = the CRP diffusion coefficient and D_L = the LDL diffusion coefficient or said $c_n = 1.0$ mg/L for adult and said $F = 0.66$;

substituting said c_m , said c_n and said F into the following expression where $c_m \geq c_n$:

$$R_2 = F \left(\left(\frac{c_m}{c_n} \right)^{\frac{11}{9}} - 1 \right) \quad (3)$$

and

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calculating (3) yields said disease risk R_2 caused by said CRP concentration parameter related to the atherosclerotic risk factors being an elevated CRP level in human blood plasma, systemic inflammation, infectious agents or other risk factors that increase said CRP level.

Claim 4 (Original): A method as in claim 1 wherein determining said disease risk yielded by the difference between the measured value and the normal value of said blood systolic pressure parameter, said method comprising the steps of:

a measured value, p_m in mmHg, of the individual's blood systolic pressure is determined using a medical technique for measuring the human blood pressure or said p_m is determined by the physician;

a normal value, p_n in mmHg, of said systolic pressure is determined by the physician or said $p_n = 120$ mmHg for adult;

substituting said p_m and said p_n into the following expression where $p_m \geq p_n$:

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$$R_4 = \left(\frac{P_m}{P_n} \right)^{\frac{1}{3}} - 1 \quad (4)$$

and

calculating (4) yields said disease risk R_4 caused by said systolic pressure parameter related to the atherosclerotic risk factors being an elevated level of blood systolic pressure, family history of hypertension or other risk factors that increase said systolic pressure.

Claim 5 (Original): A method as in claim 1 wherein determining said disease risk yielded by the difference between the measured value and the normal value of said blood diastolic pressure parameter, said method comprising the steps of:

a measured value, p_m in mmHg, of the individual's blood diastolic pressure is determined using a medical technique for measuring the human blood pressure or said p_m is determined by the physician;

a normal value, p_n in mmHg, of said blood diastolic pressure is determined by the physician or said $p_n = 70$ mmHg for adult;

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substituting said p_m and said p_n into the following expression where $p_m \geq p_n$:

$$R_s = \left(\frac{p_m}{p_n} \right)^{\frac{1}{3}} - 1 \quad (5)$$

and

calculating (5) yields said disease risk R_s caused by said diastolic pressure parameter related to the atherosclerotic risk factors being an elevate level of blood diastolic pressure, family history of hypertension or other risk factors that increase said diastolic pressure.

Claim 6 (Original): A method as in claim 1 wherein determining said disease risk yielded by the difference between the measured value and the normal value of said heart rate parameter, said method comprising the steps of:

a measured value, f_m in s^{-1} , of the individual's heart rate is determined using a medical technique for measuring the human heart rate or said f_m is determined by the physician;

a normal value, f_n in s^{-1} , of said heart rate is determined by the physician or said $f_n = 72$ per

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minute for adult;

substituting said f_m and said f_n into the following expression where $f_m > f_n$:

$$R_6 = \left(\frac{f_m}{f_n} \right)^{\frac{2}{9}} - 1 \quad (6)$$

and

calculating (6) yields said disease risk R_6 caused by said heart rate parameter related to the atherosclerotic risk factors being an elevated level of heart rate, smoking cigarette, depression or other risk factors that increase said heart rate.

Claim 7 (Original): A method as in claim 1 wherein determining said disease risk yielded by the difference between the measured value and the normal value of said arterial radius parameter, said method comprising the steps of:

a measured radius value, a_m in cm, of the individual's arterial vessel at the lesion-prone sites of arterial bifurcations, arterial branching, arterial curvatures or arterial tapering is determined using a medical technique for measuring the sizes of arterial

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vessels or said a_m is determined by the physician;

a normal value, a_n in cm, of said arterial radius is determined by the physician or said $a_n =$ a value between 0.2 cm and 2.2 cm for adult;

substituting said a_m and said a_n into the following expression where $a_m \geq a_n$:

$$R_1 = \left(\frac{a_m}{a_n} \right)^{\frac{2}{3}} - 1 \quad (7)$$

and

calculating (7) yields said disease risk R_1 caused by said arterial radius parameter related to the atherosclerotic risk factors being an increased size of arterial radius at said lesion-prone sites or other risk factors that increase the size of said arterial radius.

Claim 8 (Original): A method as in claim 1 wherein determining said disease risk yielded by the difference between the measured value and the normal value of said plasma temperature parameter, said method comprising the steps of:

a measured temperature value, T_m in °C, of the

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individual's plasma fluid in the region at said lesion-prone sites is determined using a medical technique for measuring the temperature of human blood plasma or said T_m is determined by the physician;

a normal value, T_n in °C, of said plasma temperature is determined by the physician or said $T_n = 37^\circ\text{C}$;

substituting said T_m and said T_n into the following expression where $T_m \geq T_n$:

$$R_s = \left(\frac{T_m}{T_n} \right)^{\frac{16}{27}} - 1 \quad (8)$$

and

calculating (8) yields said disease risk R_s caused by said plasma temperature parameter related to the atherosclerotic risk factors being an elevated temperature of said human blood plasma at said lesion-prone sites, elevated body temperature-related diseases or other risk factors that increase said plasma temperature.

Claim 9 (Original): A method as in claim 1 wherein determining said disease risk yielded by the

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difference between the measured value and the normal value of said angle parameter, said method comprising the step of:

a measured value, α_m in degree, of the angle between gravity and the average velocity of the blood fluid in the region at said lesion-prone sites is determined using a medical technique for measuring the human arterial geometries or said α_m is determined by the physician;

a normal value, α_n in degree, of said angle is determined by the physician or said $\alpha_n =$ a value between the 10° and 60° for adult;

substituting said α_m and said α_n into the following expression where $\alpha_n \geq \alpha_m$:

$$R_d = \left(\frac{\cos \alpha_m}{\cos \alpha_n} \right)^{\frac{2}{9}} - 1 \quad (9)$$

and

calculating (9) yields said disease risk R_d caused by said angle parameter related to the atherosclerotic risk factors being a reduced size of said angle or other risk factors that reduce said angle size.

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Claim 10 (Original): A method as in claim 1 wherein determining said disease risk yielded by the difference between the measured value and the normal value of said axial position parameter of the diffusional flux, said method comprising the steps of:

a measured value, z_m in cm, of the individual's axial position of diffusional flux along the inner arterial wall at said lesion-prone sites is determined using a medical technique for measuring the human arterial geometries or said z_m is determined by the physician;

a normal value, z_n in cm, of said axial position is determined by the physician or said $z_n =$ a value between 0.10 cm and 1.00 cm;

substituting said z_m and said z_n into the following expression where $z_m \leq z_n$:

$$R_{10} = \left(\frac{z_n}{z_m} \right)^{\frac{2}{9}} - 1 \quad (10)$$

and

calculating (10) yields said disease risk R_{10} caused by said axial position parameter related to the atherosclerotic risk factors being a

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decrease in said axial position of the diffusional flux or other risk factors that decrease said axial position.

Claim 11 (Currently amended): A method as in claim 1 ~~wherein having said nine atherosclerotic parameters-caused nine disease risks and adding said R_1 in claim 2 through said R_{10} in claim 10 all nine disease risks together so as to yields~~ yield a total risk of said disease consisting;

a current total risk of said disease related to the currently measured values of said atherosclerotic parameters; and

a previous total risk of said disease related to the previously measured values of said atherosclerotic parameters.

Claim 12 (Currently amended): A method as in claim 1 ~~wherein~~ having said total risk of said disease and determining said disease risk level containing said total risk of said disease ~~in claim 11~~, said method comprising the steps of:

dividing the disease risk level into the following seven risk sublevels: $0.84 \geq$ first

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disease risk level ≥ 0.00 , $1.75 \geq$ second
disease risk level > 0.84 , $2.70 \geq$ third disease
risk level > 1.75 , $3.70 \geq$ fourth disease risk
level > 2.70 , $4.70 \geq$ fifth disease risk level $>$
 3.70 , $5.80 \geq$ sixth disease risk level > 4.70
and seventh disease risk level > 5.80 ; and

selecting a disease risk level containing said
total risk of said disease ~~in claim 11~~ from
among seven of said disease risk sublevels.

Claim 13 (Currently amended): A method as in
claim 1 ~~wherein~~ having said total risk of said
disease and selecting an atherosclerotic risk factor
related to the atherosclerotic parameter ~~that is~~
having the greatest contribution to said total risk
of said disease ~~in claim 11~~ so as to result in said
risk factor as a primary therapy target of said
disease.

Claim 14 (Currently amended): A method as in
claim 1 ~~wherein~~ having said LDL concentration
parameter-caused the disease risk R_1 and said CRP
concentration parameter-caused the disease risk R_2
and selecting said greater flux between said LDL mass
transfer flux and said monocyte mass transfer flux so

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as to result in said greater flux as a primary cause in said disease, said method comprising the steps of:

selecting said LDL mass transfer flux as a primary cause in said disease when said R_1 ~~in claim 2~~ \geq said R_2 ~~in claim 3~~; or

selecting said monocyte mass transfer flux as a primary cause in said disease when said R_1 ~~in claim 2~~ $<$ said R_2 ~~in claim 3~~.

Claim 15 (Currently amended): A method as in claim 1 ~~wherein~~ having said LDL concentration parameter-caused the disease risk R_1 and said CRP concentration parameter-caused the disease risk R_2 and selecting said greater concentration level between said LDL level in human serum and said CRP level in human blood plasma so as to result in said greater level as a secondary therapy target, said method comprising the steps of:

selecting said LDL level in serum as a secondary therapy target of said disease when said R_1 ~~in claim 2~~ \geq said R_2 ~~in claim 3~~; or

selecting said CRP level in blood plasma as a secondary therapy target of said disease when

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said R_1 ~~in claim 2~~ < said R_2 ~~in claim 3~~.

Claim 16 (Currently amended): A method as in claim 1 ~~wherein having said current total risk of said disease and said previous total risk of said disease and~~ determining said relative ratio between said current total risk of said disease and said previous total risk of said disease ~~in claim 11~~ so as to yield said relative ratio as a therapeutic efficacy of said disease.

Claim 17 (Currently amended): A method as in claim 1 wherein ~~repeating said method in claim 2 through said method in claim 16~~ all the methods in said all processes in claim 1 are repeated until said disease risk level ~~in claim 12~~ is reduced to a normal level for said individual who requires the therapy to prevent or to treat atherosclerosis-related CHD or stroke.

Claim 18 (Currently amended): A method as in claim 1 wherein ~~said method in claim 2 through said method in claim 16~~ all the methods in said all processes in claim 1 are written as an executable computer program named said MMA.exe, or another name, to be installed into a general purpose digital computer device to accomplish said methods and to

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output a result of said methods to a display or a memory or another computer on a network, or to a user comprising:

starting the MMA.exe program on said device;

inputting the currently measured values, the previously measured values and the normal values of the individual's atherosclerosis parameters into the input screen of said MMA.exe by using the keyboard of said device;

clicking the "update" button and the "calc. risk" button of said input screen;

clicking the "evaluate" button of the MMA.exe output screen; and

outputting said output screen to a display or a memory or another computer on a network, or to a user by said computer device so as to produce a result of said methods, called the screening report containing a total risk of said disease, a disease risk level, a primary cause in said disease, a primary therapy target of said disease, a secondary therapy target of said disease and a therapeutic efficiency, to an

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individual who requires the diagnosis, the prevention or the treatment of atherosclerosis-related CHD or stroke.